

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No. : 10/600,266
Applicant(s) : Fumitoshi Asai et al
Filed : June 20, 2003
For : Medicinal Compositions Containing Aspirin
Group Art Unit : 1629
Examiner : Leslie A Royds Draper
Docket No. : 17620.105003
Confirmation No.: 7488

DECLARATION UNDER 37 CFR 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

The below named declarants hereby declare the following:

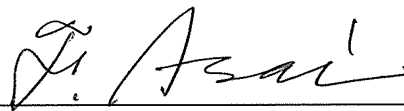
1. We are each a co-inventor of the invention described and claimed in the above-identified application.
2. Attached hereto are copies of notebook records documenting experiments done by us (the inventors) or under our supervision and control, showing reduction to practice of the claimed invention. English-language translations of these documents are also attached. The dates on the attached copies have been redacted. The dates deleted from the attachments are prior to November 3, 1998.
3. The code "CS-747", "CS747", and "747", which appear throughout the attached copies of the notebook page are our internal code for the compound identified as "Compound A" in the specification of the above-identified application.

4. The acts described in the attached documents report work done in Japan which occurred prior to November 3, 1998.


5. This Declaration under 37 CFR 1.131 is essentially the same declaration signed by Dr. Asai on October 11, 2007 and filed in U.S. Application Serial No. 10/600,266. It has now recently come to our attention that the copies of the Japanese language notebook pages that were affixed to the final version of the previous declarations which were filed in the United States Patent and Trademark Office in October 2007 were missing the even numbered notebook pages. However, the English language translation of the Japanese language notebook pages that was also affixed to the declarations and that was filed with the original declarations included translations of the missing Japanese language notebook pages. The copies of the Japanese language notebook pages attached to this present declaration contains both odd and even numbered pages and is a complete set of the notebook pages translated and attached to the declaration as well. The English language translation is the same as that previously submitted in October 2007. The error that resulted in the missing notebook pages occurred without deceptive intent.

We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Date: 11/24/2011


Fumitoshi Asai, Ph.D.


Date: 11/24/2011


Atsuhiro Sugidachi, Ph.D

Date: 11 / 29 / 2011


Taketoshi Ogawa, Ph.D

Date: 11 / 21 / 2011


Teruhiko Inoue

Attachment: Notebook records and
English translation thereof

145

CS 747

+

Aspirin

併用 Exp. 行う。

Dose

CS 747

0.3 mg/kg (4hr) まで 約 40 mg

1 mg/kg (4hr) まで 約 20

出血時間, 凝集 なども行う。3 dose は

Aspirin ⑩ + CS 747 ⑥ 2hr

まず Aspirin ⑩ + CS 747 ⑥ を中心として行う。

もし 12 ③ ④ ... ① は 多少 効きもたつて ③ と行う。

ラット動静脈シャント血栓モデル (CS-747とaspirinの併用効果検討)

【目的】

ラット動静脈シャント血栓モデルを用いてCS-747とaspirinの併用効果を検討する。

【実験期間】

に入荷のラット (36匹) を用いる。

【動物】

雄性SD系ラット (日本SLC)。7週齢で購入し、約1週間予備飼育の後実験に用いる。実験は1群6匹として行う。

【薬物】

CS-747 (宇部興産合成、Lot No. 16) およびaspirin (Sigma、A-5376、Lot No. 46H1053、入荷) を用いる。薬物は5%アラビアゴム (Sigma、Lot No. 73H0705、開封) 溶液に溶解あるいは懸濁させ、1 ml/kgの割合で動静脈シャント開通の2時間前に経口投与する。投与群は、(A) vehicle、(B) aspirin 10 mg/kg、(C) CS-747 0.3 mg/kg、(D) CS-747 0.6 mg/kg、(E) aspirin 10 mg/kg + CS-747 0.3 mg/kg、(F) aspirin 10 mg/kg + CS-747 0.6 mg/kgとする。

【方法】

(1) 実験はUmetsuらの方法 (Thromb. Haemost. 39, 74-83, 1978) を部分的に改変して行なう。

(2) 動静脈シャントに用いるチューブを以下のように作製する。長さ12 cmのメディカルシリコンチューブ (内径1.5 mm、外径2.5 mm、カネカメディックス) の両端に7 cmのシリコン (L-25、富士システムズ⁵処理したポリエチレンチューブ (内径0.5 mm、外径1.0 mm、夏目製作所) を取り付ける。ジョイントとして0.7 cmに切断したメディカルシリコンチューブ (内径1.0 mm、外径1.5 mm、カネカメディックス) を用い、接続部は血液が漏れないように外科用接着剤(ア

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ロンアルファA、三共)で接着する。また12 cmのチューブ内に10 cmの絹糸
(3-0、日腸工業)を設置する。

(3) 動静脈シャント開始2時間前に、vehicle (5%アラビアゴム溶液) または薬物
を1 ml/kgの割合で経口投与する。1群6匹の実験を行う。

(4) あらかじめ作成しておいた上記チューブに30 unit/kgとなるように、生理食
塩液 (太塚) で希釈したヘパリン溶液 (日本薬局方ヘパリンナトリウム注射液、
扶桑薬品工業、Lot No. 97H28A、XXXXXXXXXX 入荷) を満たす。

(5) 生理食塩液で40 mg/mlに希釈したペントバルビタール溶液 (ネンブタール®、
Abbott、Lot No. 20-975-Z7) を1 ml/kg腹腔内投与 (40 mg/kg) してラットを麻酔
させる。仰臥位に固定させた後、頸静脈を露出させ、シャント用チューブの片
側 (糸の付いていない方) をカニュレーションする。続いて、クレンメで血流
を遮断しておいた頸動脈に、チューブの反対端をカニュレーションし、動静脈
シャントを形成する。

(6) クレンメをはずしてシャントに30分間血液を循環させた後、絹糸に付着し
た血栓の湿重量を測定する。測定重量から糸の重量 (6.5 mg) を差し引き血栓
重量を求める。

ファイル AV-shunt (3) に保存。
(F005157-7)

XXXXXXXXXX A. Sigstam

ラッ

7

ケ
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ラット AV shunt 血圧モデル
(アスピリンと CS747 併用)

700トコ-ル P146, 147

試薬等 p110, p138

ケージ番号: 67C3-01-04

性別、系統: ♂ SD

周年令: 7週

体重:

業者名: 日本SLC

入荷日:

実験者: 杉立 収寛

飼育期間:

受付番号: 034163

匹数: 36

ラット

SD ♂ (日本SLC)

7wks 入荷

受付 No. 034163

杉立

57.7 mg アスピリン
16.2 mg CS747

1011.7 mg アスピリン

10.7 mg CS747

1024.7 mg アスピリン

5% Arabic gum soln.

$50 \text{ mg/ml} = 1011.7 \text{ mg} / 20.234 \text{ ml dH}_2\text{O}$

Aspirin

$10 \text{ mg/ml} = 57.7 \text{ mg} / 5.77 \text{ ml } 5\% \text{ アスピリン soln.}$

CS747

$16.2 \text{ mg} / 5.4 \text{ ml} = 3 \text{ mg/ml}$

$3 \text{ mg/ml soln } 1 \text{ ml} + 5\% \text{ アスピリン soln. } 2 \text{ ml} = 1 \text{ mg/ml}$

$1 \text{ mg/ml soln. } 1 \text{ ml} + 5\% \text{ アスピリン soln. } 2.33 \text{ ml} = 0.3 \text{ mg/ml}$

$1 \text{ mg/ml soln. } 1.5 \text{ ml} + 5\% \text{ アスピリン soln. } 1 \text{ ml} = 0.6 \text{ mg/ml}$

上記の2つを5:12で作る (正確に)

$5\% \text{ アスピリン } 1024.7 \text{ mg} / 21.69 \text{ ml dH}_2\text{O} = 50 \text{ mg/ml}$

CS747 $10.7 \text{ mg} / 10.7 \text{ ml アスピリン soln.} = 1 \text{ mg/ml}$

$1 \text{ mg/ml soln. } 1.5 \text{ ml} + 5\% \text{ アスピリン soln. } 3.5 \text{ ml} = 0.3 \text{ mg/ml}$

$1 \text{ mg/ml soln. } 3 \text{ ml} + 5\% \text{ アスピリン soln. } 2 \text{ ml} = 0.6 \text{ mg/ml}$

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	B.W. (g)	Treatment	測定値 (ms)	Thrombus (mg)	
#1	253	Vehicle	61.3	54.8	
2	252	Aspirin (10)	51.3	44.8	#1
3	262	CS747 (0.3)	58.3	51.8	
4	267	CS747 (0.6)	43.1	36.6	
5	256	Aspirin (10) + CS747 (0.3)	39.6	33.1	
6	271	Aspirin (10) + CS747 (0.6)	23.2	16.7	
7	250	V	63.2	56.7	#2
8	246	A (10)	58.4	51.9	
9	258	747 (0.3)	51.8	45.3	
10	269	747 (0.6)	53.1	46.6	
11	268	A (10) + 747 (0.3)	30.5	24.0	#3
12	244	A (10) + 747 (0.6)	41.3	34.8	
13	247	V	56.1	48.6	
14	262	A (10)	48.6	42.1	
15	256	747 (0.3)	52.2	45.7	
16	267	747 (0.6)	46.3	39.8	#4
17	268	A (10) + 747 (0.3)	42.2	35.7	
18	242	A (10) + 747 (0.6)	21.6	15.1	

#1 252.9g
251.7g
262.3g
267.3g
256.4g
271.1g

#7 250.0g
245.8g
257.8g
269.0g
268.3g
244.4g

#13 247.0g
262.3g
256.2g
267.3g
267.6g
242.1g

V = vehicle
A = Aspirin
747 = CS747

ヘリウム

1000 u/ml soln. 1ml + saline 9ml = 100 unit/ml

100 u/ml soln. 3ml + saline 7ml = 30 unit/ml

#5

#6

#1 0.0613 g

#7 0.0632 g

#13 0.0561 g

#2 0.0513 g

#8 0.0584 g

#14 48.6 mg

#3 0.0583 g

#9 0.0518 g

#15 52.2 mg

#4 0.0431 g

#10 0.0531 g

#16 0.0463 g

#5 0.0396 g

#11 0.0305 g

#17 0.0422 g

#6 0.0232 g

#12 41.3 mg

#18 0.0216 g

unit/ml

e

A. Sugidaru

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ラット AV shut 血栓モデル
(アスピリン + CS747)

CS747

700 | コール p146, 147 試験番号 p110, 118

ケージ番号: 65C3-01-01

性別、系統: ♂ SD

周年令: 7週

体重:

業者名: 日本SLC

入荷日:

実験者: 杉立 収寛

飼育期間:

受付番号: 034163

6

36 + 2

匹数: 36

ラット

SD ♂ (7wks入荷)

日本SLC

入荷

杉立

受付番号 034163

A.W.

B.W.

#1 271

2 278

3 273

4 275

5 246

6 252

7 281

8 264

9 253

10 248

11 263

12 263

13 271

14 265

15 266

16 256

17 246

18 272

おまけ2匹

↓

Cozgas 2匹

±セ

B.W.

72.0 mg

11.3 mg

#1 271.0g

277.6g

272.8g

275.0g

245.5g

#6 251.6g

#10 248.2g

#8 263.9g

#9 253.3g

#7 281.1g

#11 263.4g

#12 263.4g

#13 271.3g

265.3g

266.0g

255.5g

245.6g

#18 272.4g

1224.1 mg

5%アスピリン = 50 mg/ml

= 1224.1 / 24.48 ml dH₂O

Aspirin

10 mg/ml = 72.0 / 7.2 ml 5%アスピリン soln.

CS 747 { $11.3 \text{ mg} / 11.3 \text{ ml} \quad 5\% \text{ アスピリン soln.} = 1 \text{ mg/ml}$
 $1 \text{ mg/ml soln.} \quad 1.5 \text{ ml} + 5\% \text{ アスピリン soln.} \quad 1 \text{ ml} = 0.6 \text{ mg/ml}$
 $1 \text{ mg/ml soln.} \quad 1 \text{ ml} + 5\% \text{ アスピリン soln.} \quad 2.33 \text{ ml} = 0.7 \text{ mg/ml}$

1100) ✓ $1000 \text{ unit/ml soln. (original)} \quad 1 \text{ ml} + \text{saline } 9 \text{ ml} = 100 \text{ unit/ml}$

荷) $100 \text{ unit/ml soln.} \quad 3 \text{ ml} + \text{saline } 7 \text{ ml} = 30 \text{ unit/ml}$

	B.W. (g)	Treatment	出血値 (ms)	Thrombus (mg)
63	#1 271	V	55.6	49.1
	2 278	A⑩	52.9	46.4
	3 273	747⑦	43.9	37.4
	4 275	747⑥	41.0	34.5
	5 246	A⑩ + 747⑦	24.6	18.1
	6 252	A⑩ + 747⑥	19.7	13.2
安楽死	7 281	V	59.0	52.5
	8 264	A⑩	63.2	56.7
	9 253	747⑦	47.1	40.6
	10 248	747⑥	38.5	32.0
	11 263	A⑩ + 747⑦	36.7	30.2
	12 263	A⑩ + 747⑥	35.6	29.1
	13 271	V	57.8	51.3
	14 265	A⑩	44.3	37.8
	15 266	747⑦	46.4	39.9
	16 256	747⑥	42.2	35.7
	17 246	A⑩ + 747⑦	48.3	41.8
	18 272	A⑩ + 747⑥	36.6	30.1

1h. { $V = \text{Vehicle}$
 $A = \text{Aspirin}$
 $747 = \text{CS-747}$

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#1 0.0556 g

#7 0.0590 g

#13 0.0578 g

#2 0.0529 g

#8 0.0632 g

#14 44.3 mg

#3 0.0439 g

#9 0.0471 g

#15 0.0464 g

#4 0.0410 g

#10 0.0385 g

#16 42.2 mg

#5 0.0246 g

#11 0.0367 g

#17 48.3 mg

#6 0.0197 g

#12 0.0356 g

#18 36.6 mg

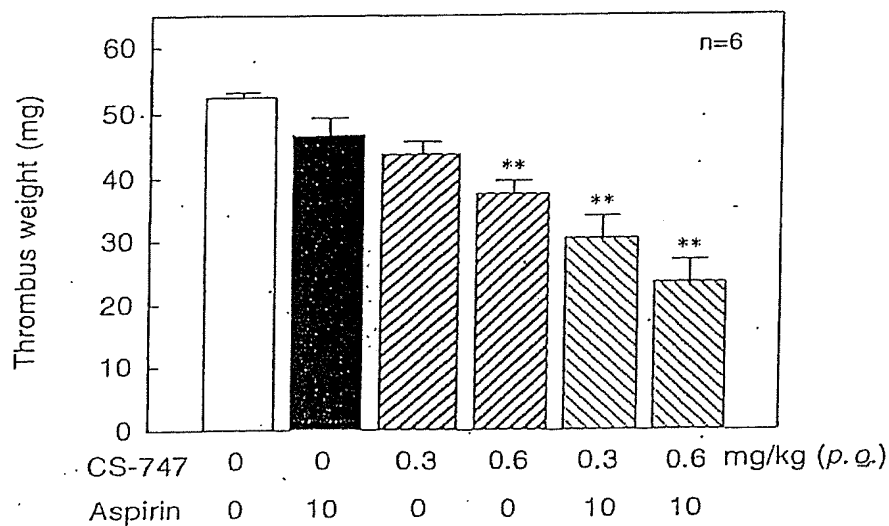
Aspirin +

V.

A. Sugrathaw



Arterio-venous shunt thrombosis model in rats



Aspirin + CS747 fed

vehicle	52.3 ± 1.2
Aspirin (10)	46.6 ± 2.8
CS747 (0.3)	43.5 ± 2.1
CS747 (0.6)	37.5 ± 2.1
Aspirin (10) + CS747 (0.3)	30.5 ± 3.5
Aspirin (10) + CS747 (0.6)	27.2 ± 3.8

A. Sugidanti

[REDACTED]

CS 747

+

Combination Experiment

Aspirin

Dose	CS 747	0.3 mg/kg (4hr)	about 40 mg
		1 mg/kg (4hr)	about 20

Dose in which both bleeding time and aggregation were measured:

Aspirin 10 + CS 747 0.6 2hr

First, experiment with a central focus on Aspirin 10 + CS 747 0.6

Another group 0.3 or 1

Conduct 0.3 because 1 seems to work too much.

Arterio-venous Shunt Thrombosis Model in Rats
(Examination of effect by combination of CS-747 with aspirin)

[Object]

Examine the effect by combination of CS-747 with aspirin using Arterio-venous shunt thrombosis model in rats.

[Experimental Term]

Thirty six rats received on [REDACTED] are used.

[Animals]

Seven-week-old male SD rats (Japan SLC) are purchased and used for the experiment after preliminary breeding for about a week. The experiment is conducted as 6 rats per group.

[Test agents]

CS-747 (synthesized by Ube Industrials Ltd., Lot No. 16) and aspirin (Sigma, A-5376, Lot No. 46H1053, received on [REDACTED]) are used. The test agents are dissolved or suspended in a 5% Arabic gum (Sigma, Lot No. 73H0705, opened on [REDACTED]) solution and administered orally in volume of 1 ml/kg two hours before starting arterio-venous shunt. Administered group are (A) vehicle, (B) aspirin 10 mg/kg, (C) CS-747 0.3 mg/kg, (D) CS-747 0.6 mg/kg, (E) aspirin 10 mg/kg + CS-747 0.3 mg/kg, and (F) aspirin 10 mg/kg + CS-747 0.6 mg/kg.

[Methods]

(1) For the experiment, the method by Umetsu et al. (Thromb. Haemost. 39, 74-83, 1978) is partly modified.

(2) The shunt tube for arterio-venous shunt is prepared as follows: both sides of a medical silicon tube of 12 cm length (inner diameter: 1.5 mm, outer diameter: 2.5 mm, KANEKA Medix Co., Ltd) are connected each to a polyethylene tube of 7 cm length (inner diameter: 0.5 mm, outer diameter: 1.0 mm, Natsume Seisakusho Co., Ltd.)

covered with silicon via a medical silicon tube of 0.7 cm length (inner diameter: 1.0 mm, outer diameter: 1.5 mm, KANEKA Medix Co., Ltd.) as connector. At the connection,

Page 147

[REDACTED]

surgical adhesive (Aronalpha A, Sankyo) is used for preventing blood leak. In addition, a silk thread (size 3-0, Niccho Kogyo) of 10 cm length is placed in the tube of 12 cm length.

(3) Vehicle (5% Arabic gum solution) or test agents are administered orally in a volume of 1 ml/kg 2 hours before starting arterio-venous shunt. 6 rats per group are used.

(4) The above tube prepared in advance is filled with heparin solution (Japanese Pharmacopoeia Heparin Sodium Injection, Fuso Pharmaceutical Industries, Ltd., Lot No. 97H28A, received on [REDACTED]) diluted with normal saline (Otsuka) resulting in 30 unit/kg.

(5) The rat is anesthetized with an intraperitoneal injection of 1 ml/kg (40 mg/kg) of pentobarbital solution (Nembutal R, Abbott, Lot No. 20-975-Z7) diluted with normal saline resulting in 40 mg/ml. After it is fixed to turning up, the jugular vein is exposed and one side of the shunt tube (in which the silk thread is not adhered) is cannulated. Subsequently, to the carotid artery where bloodstream is shut using clamp, the other side of the tube is cannulated to make the arterio-venous shunt.

(6) After removing the clamp and allowing blood to circulate for 30 minutes, the thrombus adsorbed on the silk thread is weighed. The thrombus weight was calculated by subtracting of the weight of the thread (6.5 mg) from the measured weight.

Files were stored at AV-shunt (3) (F00515 data)

[REDACTED] A. Sugidachi

AV shunt Thrombosis Model in Rats
(Combination of CS 747 with aspirin)

Protocol: P. 146, 147

Reagent and so on: p. 110, p. 138

Cage number: 6raC3-01-04

Rats

SD male (Japan SLC)

Sex, system: male SD

██████████ wks, Receipt

Year-round old: 7 weeks

Receipt number: 034163

Body weight:

Sugidachi

Manufacture name: Japan SLC

Receive date: ██████████

Number of rats: 36

Experimenter: Atsuhiko Sugidachi

Housing term: ██████████ to ██████████

Receipt number: 034163

57.7mg aspirin 5% Arabic gum soln.
16.2 mg CS 747 50 mg/ml = 1011.7 mg / 20.234 ml dH₂O

Aspirin
10 mg/ml = 57.7 mg / 5.77 ml 5% Arabic gum soln.
1011.7 mg Arabic gum

CS 747
16.2 mg / 5.4 ml = 3 mg/ml
3 mg/ml soln. 1 ml + 5% Arabic gum soln. 2 ml = 1 mg/ml
1 mg/ml soln. 1 ml + 5% Arabic gum soln. 2.33 ml = 0.3 mg/ml
1 mg/ml soln. 1.5 ml + 5% Arabic gum soln. 1 ml = 0.6 mg/ml
10.7 mg CS 747 Further prepared because of insufficient (spilled)
5% Arabic gum 1084.7 mg / 21.69 ml dH₂O = 50 mg/ml
1084.7 mg Arabic gum CS 747 10.7 mg / 10.7 ml Arabic gum soln. = 1 mg/ml
1 mg/ml soln. 1.5 ml + 5% Arabic gum soln. 3.5 ml = 0.3 mg/ml
1 mg/ml soln. 3 ml + 5% Arabic gum soln. 2 ml = 0.6 mg/ml

	B. W. (g)	Treatment	Measured value (mg)	Thrombus (mg)
#1	253	Vehicle	61.3	54.8
2	252	Aspirin $\boxed{10}$	51.3	44.8
3	262	CS 747 $\boxed{0.3}$	58.3	51.8
4	267	CS 747 $\boxed{0.6}$	43.1	36.6
5	256	Aspirin $\boxed{10}$ + CS 747 $\boxed{0.3}$	39.6	33.1
6	271	Aspirin $\boxed{10}$ + CS 747 $\boxed{0.6}$	23.2	16.7
7	250	V	63.2	56.7
8	246	A $\boxed{10}$	58.4	51.9
9	258	747 $\boxed{0.3}$	51.8	45.3
10	269	747 $\boxed{0.6}$	53.1	46.6
11	268	A $\boxed{10}$ + 747 $\boxed{0.3}$	30.5	24.0
12	244	A $\boxed{10}$ + 747 $\boxed{0.6}$	41.3	34.8
13	247	V	56.1	49.6
14	262	A $\boxed{10}$	48.6	42.1
15	256	747 $\boxed{0.3}$	52.2	45.7
16	267	747 $\boxed{0.6}$	46.3	39.8
17	268	A $\boxed{10}$ + 747 $\boxed{0.3}$	42.2	35.7
18	242	A $\boxed{10}$ + 747 $\boxed{0.6}$	21.6	15.1

V = Vehicle

A = Aspirin

747 = CS 747

heparin

1000 u/ml soln. 1 ml + saline 9 ml = 100 unit/ml

100 u/ml soln. 3 ml + saline 7 ml = 30 unit/ml

#1 252.9 g
251.7 g
262.3 g
267.3 g
256.4 g
271.1 g

#7 250.0 g
245.8 g
257.8 g
269.0 g
268.3 g
244.4 g

#13 247.0 g
262.3 g
256.2 g
267.3 g
267.6 g
242.1 g

[REDACTED]

#1	0.0613 g	#7	0.0632 g	#13	0.0561 g
#2	0.0513 g	#8	0.0584g	#14	48.6 mg
#3	0.0588 g	#9	0.0518 g	#15	52.2 mg
#4	0.0431 g	#10	0.0531 g	#16	0.0463 g
#5	0.0396 g	#11	0.0305 g	#17	0.0422 g
#6	0.0232 g	#12	41.3 mg	#18	0.0216 g

[REDACTED]

A. Sugidachi

AV Shunt Thrombosis Model in Rats
(Aspirin + CS 747)

Protocol: p. 146, 147

Reagents and so on: p. 110, 138

Cage number: 6raC3-01-01 Rat
SD male (7 wks, Receipt)
Sex, system: male SD 36+2 Japan SLC
Year-round old: 7 weeks Receipt
Body weight: Sugidachi
Manufacture name: Japan SLC Receipt number: 034163
Receive date: Number of rats: 36
Experimenter: Atsuhiko Sugidachi
Housing term: to
Receipt number: 034163

Additional 2 rats

↓

euthanasia using CO₂ gas

#1	B. W. .	72.0 mg
	271.0 g	11.3 mg
	277.6 g	
	272.8 g	
	275.0 g	
	245.5 g	
#6	251.6 g	1224.1 mg
#10	248.2 g	
#8	263.9 g	
#9	253.3 g	
#7	281.1 g	
#11	263.4 g	5% Arabic gum = 50 mg/ml
#12	263.4 g	= 1224.1 / 24.48 ml dH ₂ O
#13	271.3 g	
	265.3 g	Aspirin
	266.0 g	
	255.5 g	10 mg/ml = 72.0 / 7.2 ml 5% Arabic gum soln.
	245.6 g	
#18	272.4 g	

CS 747 11.3 mg / 11.3 ml 5% Arabic gum soln. = 1 mg/ml
 1 mg/ml soln. 1.5 ml + 5% Arabic gum soln. 1ml = 0.6 mg/ml
 1 mg/ml soln. 1 ml + 5% Arabic gum soln. 2.33 ml = 0.3 mg/ml

heparin 1000 unit/ml soln. (origine) 1 ml + saline 9 ml = 100 unit/ml
 100 unit/ml soln. 3 ml + saline 7 ml = 30 unit/ml

	B. W. (g)	Treatment	Measured value (mg)	Thrombus (mg)
#1	271	V	55.6	49.1
2	278	A 10	52.9	46.4
3	273	747 0.3	43.9	37.4
4	275	747 0.6	41.0	34.5
5	246	A 10 + 747 0.3	24.6	18.1
6	252	A 10 + 747 0.6	19.7	13.2
7	281	V	59.0	52.5
8	264	A 10	63.2	56.7
9	253	747 0.3	47.1	40.6
10	248	747 0.6	38.5	32.0
11	263	A 10 + 747 0.3	36.7	30.2
12	263	A 10 + 747 0.6	35.6	29.1
13	271	V	57.8	51.3
14	265	A 10	44.3	37.8
15	266	747 0.3	46.4	39.9
16	256	747 0.6	42.2	35.7
17	246	A 10 + 747 0.3	48.3	41.8
18	272	A 10 + 747 0.6	36.6	30.1

V = Vehicle

A = Aspirin

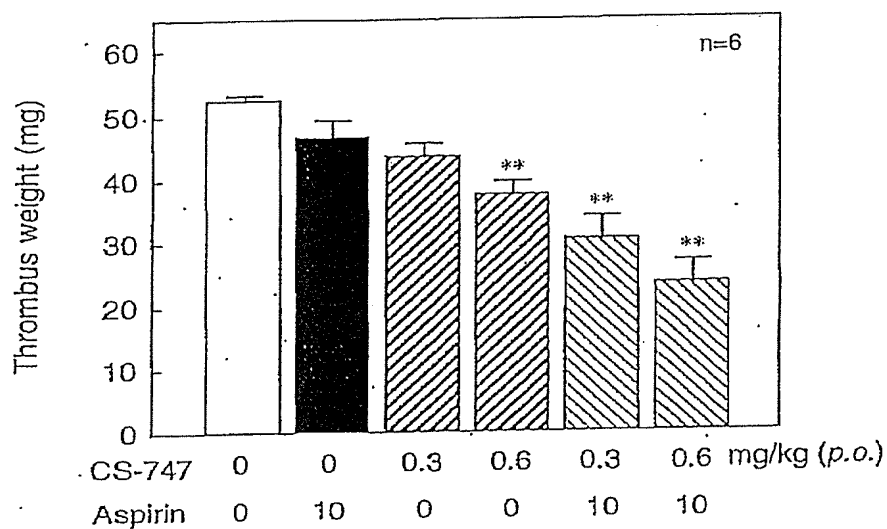
747 = CS 747

#1	0.0556 g	#7	0.0590 g	#13	0.0578 g
#2	0.0529 g	#8	0.0632 g	#14	44.3 mg
#3	0.0439 g	#9	0.0471 g	#15	0.0464 g
#4	0.0410 g	#10	0.0385 g	#16	42.2 mg
#5	0.0246 g	#11	0.0367 g	#17	48.3 mg
#6	0.0197 g	#12	0.0356 g	#18	36.6 mg

[REDACTED] A. Sugidachi

Hirose [REDACTED]

Arterio-venous shunt thrombosis model in rats



Aspirin + CS 747 Summary

Vehicle	52.3 ± 1.2
Aspirin 10	46.6 ± 2.8
CS 747 0.3	43.5 ± 2.1
CS 747 0.6	37.5 ± 2.1
Aspirin 10 + CS 747 0.3	30.5 ± 3.5
Aspirin 10 + CS 747 0.6	23.2 ± 3.8